

CLAIMS

1. A method of preparing a porphyrin derivative starting from a meso-substituted porphyrin compound, **characterized** in that a meso-(2'-cyanovinyl)-substituted porphyrin compound of which the vinyl is optionally substituted is used as the meso-substituted porphyrin compound, wherein said meso-(2'-cyanovinyl)-substituted porphyrin compound, in a form in which its porphyrin macrocycle is complexed with a bivalent metal ion

i) is subjected to

an acid for which $0 < \text{pKa} < 5$

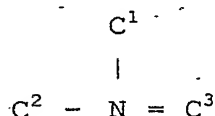
and

an oxidising agent,

with the restriction that if the carbon atom of the porphyrin macrocycle at which the (2'-cyanovinyl) substituent is attached is designated $\text{C}\alpha$, there must be a substituent attached to $\text{C}\delta$, counting along the perimeter of the porphyrin macrocycle, said substituent comprising a -C-C motif directly attached at the $\text{C}\delta$ carbon atom;

or

ii) is subjected under aprotic conditions to a Vilsmeier reagent having a reactive motif



containing a quaternary nitrogen atom which is directly linked to two carbon atoms C^1 , C^2 wherein said carbon atoms are not part of a unsaturated or aromatic moiety, and which quaternary nitrogen atom is directly linked to a carbon atom C^3 via a double bond, said carbon atom C^3 carrying a halogen atom chosen from fluoro, chloro, bromo and iodo

with the restriction that if the carbon atom of the porphyrin macrocycle at which the (2'-cyanovinyl) substituent is attached is designated $\text{C}\alpha$, there must be a sub-

stituent attached to C δ , counting along the perimeter of the porphyrin macrocycle, said substituent comprising a -CH motif directly attached at the C δ carbon atom;

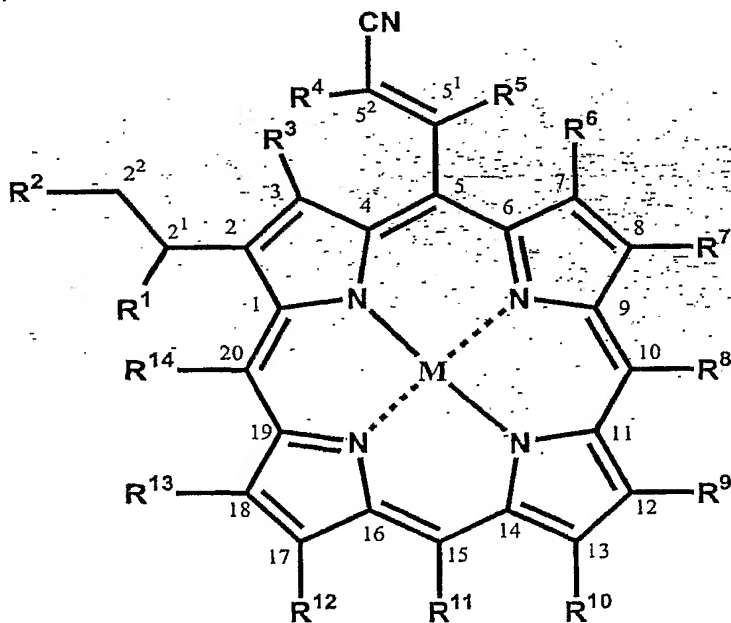
to convert said meso-(2'-cyanovinyl)-substituted porphyrin

- 5 compound into a porphyrin derivative having a quinoline-ring system peri-condensed to the porphyrin ring, and optionally the bivalent metal ion is removed or replaced by another metal ion, and optionally the nitrogen atom of the quinoline-ring system ring is quaternized.

- 10 2. The method according to claim 1, **characterized** in that for alternative step i) a meso-(2'-cyanovinyl)-substituted porphyrin compound of formula (I) is used as the starting compound,

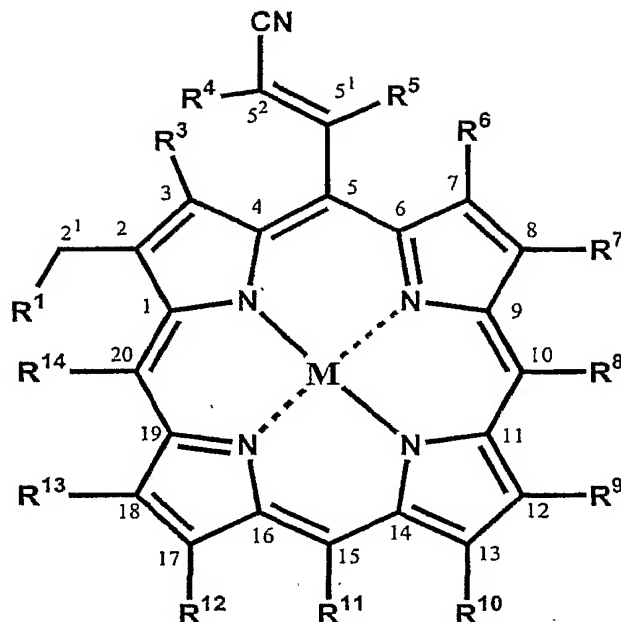
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(I)



- or wherein for alternative step ii) meso-(2'-cyanovinyl)-substituted porphyrin compound of formula (III) is used as the starting compound
- 20

(III)



wherein

- 5 R¹, R² represent independently of each other hydrogen, linear or branched (C₁₋₈) alkyl, or linear or branched (C₁₋₈) alkyl C(O)O (C₁₋₈) alkyl, wherein the groups comprising alkyl may optionally be substituted with fluoro, chloro, bromo, iodo, nitrile, (C₁₋₈) thioether, and (C₁₋₈) alkoxy;
- 10 R³ represents H or (C₁₋₈) alkyl;
- R⁴ and R⁵, represent, independently of each other, hydrogen, nitrile, monocyclic, bicyclic or tricyclic (C₆₋₁₄) aryl, or (C₁₋₄) alkyl wherein the aryl and alkyl group may optionally be substituted with fluoro, chloro, bromo, iodo, nitrile, (C₁₋₈) thioether, and (C₁₋₈) alkoxy;
- 15 R⁶ to R¹⁴ represent independently of each other, hydrogen, linear or branched (C₁₋₈) alkyl, linear or branched (C₁₋₈) alkyl C(O)O (C₁₋₈) alkyl, wherein n is an integer of 0 to 4, CH₂=CH-, a monocyclic, bicyclic or tricyclic (C₃-C₁₄) aryl, which aryl may optionally contain one or more nitrogen atoms as heteroatoms; and R⁸, R¹¹, and R¹⁴ may in addition represent an acrylonitrile group substituted with R^{4'} and R^{5'}, wherein
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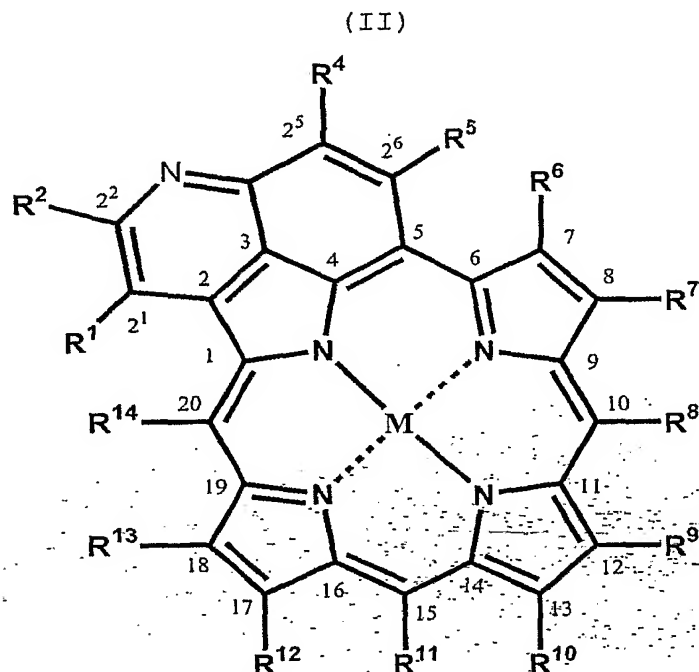
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$R^{4'}$ and $R^{5'}$ are as defined for R^4 and R^5 ;

and

M represents a bivalent metal ion,

wherein the compound of formula (I) or (III) is converted
 5 into the corresponding porphyrin derivative of formula (II)
 comprising a quinoline-ring system fused to the porphyrin
 ring



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wherein the substituents have the meanings given
 above, and depending on the meaning of R^8 , R^{11} , and R^{14} and the
 correspondence of an adjacent R^7 , R^9 , R^{10} , R^{12} , and R^{13} with R^3
 optionally more than one quinoline-ring system peri-condensed
 15 to the porphyrin ring is present.

3. The method according to claim 1 or 2, **characterized**
 in that the nitrogen atom of the peri-condensed quinoline-
 ring system ring in formula (II) is quaternized.

4. The method according to any of the preceding claims,
 20 **characterized** in that the meso-(2'-cyanovinyl)-substituted
 porphyrin compound is prepared by introducing a formyl or
 acetyl residue at a meso position of a porphyrin compound,
 whereafter the mesoformylporphyrin thus formed is converted

into the meso-(2'-cyanovinyl) derivative.

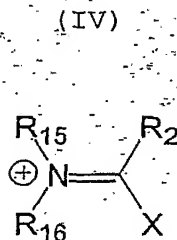
5. The method according to claim 4, **characterized** in that the mesoformylporphyrin formed is converted into the meso-(2'-cyanovinyl)-substituted porphyrin compound by reaction with diethylphosphonoacetonitril.

6. The method according to any of the preceding claims, **characterized** in that the porphyrin starting compound for the preparation of the meso-(2'-cyanovinyl) porphyrin is chosen from the group of i) hemin, and ii) heme.

7. The method according to any of the preceding claims, **characterized** in that Ni^{2+} is used as the bivalent metal ion.

8. The method according to any of the preceding claims, **characterized** in that a Brönsted-acid is used with the proviso that $0 < \text{pK}_a < 5$, the reaction being carried out at a temperature above 140°C .

9. The method according to any of the claims 1 to 7, **characterized** in that the Vilsmeier reagent used is of the formula (IV)



wherein

R15 and R16 are, independently of each other, linear or branched C_{1-8} alkyl,

X is fluoro, chloro, bromo and iodo, and

R2 is hydrogen, linear or branched (C_{1-8}) alkyl, or linear or branched (C_{1-8}) alkyl $\text{C}(\text{O})\text{O}$ (C_{1-8}) alkyl, wherein the groups comprising alkyl may optionally be substituted with fluoro, chloro, bromo, iodo, nitrile, (C_{1-8}) thioether, and (C_{1-8}) alkoxy.

10. The method according to claim 9, **characterized** in that X is chloro or bromo.

11. Porphyrin derivatives, wherein said derivatives are:

- 2'-methoxycarbonylquino[4,4a,5,6-jkl]-annulated 12-demethyl-13-de[2-(methoxycarbonyl)ethyl]mesoporphyrin dimethylester;
- 2'-methoxycarbonylquino[4,4a,5,6-qrs]-annulated 18-demethyl-17-de[2-(methoxycarbonyl)ethyl]mesoporphyrin dimethylester;
- quino[4,4a,5,6-abt]-annulated 2-demethyl-3-deethylmesoporphyrin dimethylester;
- quino[4,4a,5,6-efg]-annulated 7-demethyl-8-deethylmesoporphyrin;
- 2'-methoxycarbonylquino[4,4a,5,6-jkl]-annulated 12-demethyl-13-de[2-(methoxycarbonyl)ethyl]mesoporphyrin;
- 2'-methoxycarbonylquino[4,4a,5,6-qrs]-annulated 18-demethyl-17-de[2-(methoxycarbonyl)ethyl]mesoporphyrin;
- quino[4,4a,5,6-abt]-annulated 2-demethyl-3-deethylmesoporphyrin;
- quino[4,4a,5,6-bcd]-2-demethyl-3-deethyl-mesoporphyrin dimethylester;
- quino[4,4a,5,6-bcd]-2-demethyl-3-deethyl-mesoporphyrin;
- 3'-methylquino[4,4a,5,6-efg]-7-demethyl-8-deethylmesoporphyrin dimethylester;
- 3'-methylquino[4,4a,5,6-efg]-7-demethyl-8-deethylmesoporphyrin;
- 9'-aminocarbonylquino[4,4a,5,6-efg]-7-demethyl-8-deethylquinoporphyrin dimethylester;
- 9'-aminocarbonylquino[4,4a,5,6-efg]-7-demethyl-8-deethylquinoporphyrin
- N-benzylquinolinium[4,4a,5,6-efg]-annulated mesoporphyrin dimethylester
- N-benzylquinolinium[4,4a,5,6-efg]-annulated mesoporphyrin.

12. A porphyrin derivative having a quinoline-ring system peri-condensed to the porphyrin ring.

13. Use of a porphyrin derivative according to claim 12 for the preparation of a pharmaceutical composition of a porphyrin derivative according to the invention for prevention of and/or treating

1) benign, malignant, inflamed and infectious skin and mucosa disorders: skin/mucosa disorders;

2) vascular disorders;

3) tumors and pre-cancerous lesions;

5 4) ophthalmology disorders;

5) gynecological or urological disorders;

6) immunological disorders;

7) oral cavity or nasopharyngeal disorders.

14. Use of a porphyrin derivative according to claim 12
10 for the preparation of a composition of a porphyrin derivative according to the invention for the preparation of a composition

1) for photodetection of malignant and pre-malignant lesions;

15 2) for decontamination or pathogen reduction of liquids such biological fluids and contaminated water;

3) for decontamination or pathogen reduction of surfaces;

4) for use as insecticide.

20 15. Pharmaceutical composition comprising a porphyrin derivative according to claim 12 together with a pharmaceutically acceptable carrier or excipient.